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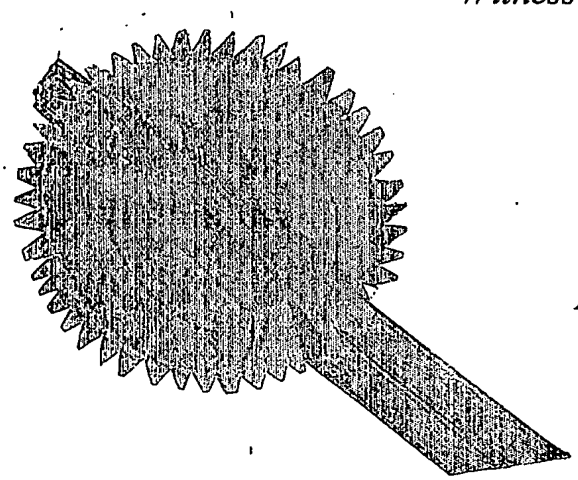
INTELLECTUAL PROPERTY INDIA

GOVERNMENT OF INDIA
MINISTRY OF COMMERCE & INDUSTRY
PATENT OFFICE, DELHI BRANCH
W - 5, WEST PATEL NAGAR
NEW DELHI - 110 008.

I, the undersigned being an officer duly authorized in accordance with the provision of the Patent Act, 1970 hereby certify that annexed hereto is the true copy of the ***Application*** *and* ***Complete Specification*** *filed in connection with Application for Patent No.**1053/Del/2003** dated 28th **August 2003**.*

Witness my hand this 16th day of November 2004.



(S.K. PANGASA)
Assistant Controller of Patents & Designs

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Chemistry
A61K 31/00
A61K 9/20

1053 DEL 03

FORM 1

THE PATENTS ACT, 1970

(39 of 1970)

APPLICATION FOR GRANT OF A PATENT

(See Sections 5(2), 7, 54 and 135; and rule 39)

1 We, **RANBAXY LABORATORIES LIMITED**, a Company incorporated under the Companies Act, 1956, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India

2. hereby declare –

(a) that we are in possession of an invention titled **"SOLID ORAL DOSAGE FORMS OF GATIFLOXACIN"**

(b) that the Complete Specification relating to this invention is filed with this application.

(c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

a. ROMI BARAT SINGH
b. PANANCHUKUNNATH MANOJ KUMAR
c. VISHNUBHOTLA NAGA PRASAD
d. SANJEEV KUMAR SETHI
e. RAJIV MALIK

of Ranbaxy Laboratories Limited, Plot No. 20, Sector-18, Udyog Vihar Industrial Area, Gurgaon – 122001 (Haryana), India, all Indian Nationals.

4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows: NOT APPLICABLE

5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which we are the applicant: **NOT APPLICABLE**

6. We state that the application is divided out of our application, the particulars of which are given below and pray that this application deemed to have been filed on ..... Under section 16 of the Act. **NOT APPLICABLE**

7. That we are the assignee or legal representatives of the true and first inventors.

8. That our address for service in India is as follows:

DR. B. VIJAYARAGHAVAN
Associate Director – Intellectual Property
Ranbaxy Laboratories Limited
Plot No.20, Sector – 18, Udyog Vihar Industrial Area,
Gurgaon – 122001 (Haryana). INDIA.

9. Following declaration was given by the inventors or applicants in the convention country:
We, ROMI BARAT SINGH, PANANCHUKUNNATH MANOJ KUMAR, VISHNUBHOTLA NAGA PRASAD, SANJEEV KUMAR SETHI, RAJIV MALIK of Ranbaxy Laboratories Limited, Plot No. 20, Sector – 18, Udyog Vihar Industrial Area, Gurgaon–122001 (Haryana), India, all Indian Nationals, the true and first inventors for this invention or applicant in the convention country declare that the applicant herein, **Ranbaxy Laboratories Limited**, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India, is our assignee or legal representatives.

a. Romi Singh

(ROMI BARAT SINGH)

b.

(PANANCHUKUNNATH MANOJ KUMAR)

c.

(VISHNUBHOTLA NAGA PRASAD)

d.

(SANJEEV KUMAR SETHI)

e.

(RAJIV MALIK)

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

11. Followings are the attachment with the application:
   a. Complete Specification (3 copies)
   b. Drawings (3 copies)
   c. Priority document(s)
   d. Statement and Undertaking on FORM – 3
   e. Power of Authority (Not required)
   f. Fee Rs.3,000/- (Rupees Three Thousand only..) in cheque bearing No.
      dated : drawn on **HDFC Bank Limited, New Delhi.**

We request that a patent may be granted to us for the said invention.

Dated this 27TH day of **August, 2003.**

For Ranbaxy Laboratories Limited

Sbay

(SUSHIL KUMAR PATAWARI)
Company Secretary

FORM 2 1057 DEL 03

The Patents Act, 1970 28 AUG 2003

(39 of 1970)

COMPLETE SPECIFICATION

(See Section 10)

SOLID ORAL DOSAGE FORMS OF GATIFLOXACIN

RANBAXY LABORATORIES LIMITED

19, NEHRU PLACE, NEW DELHI - 110019

(A Company incorporated under the Companies Act, 1956)

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

Technical Field of the Invention

The present invention relates to solid oral dosage forms of gatifloxacin having reproducible release characteristics and a process for the preparation thereof.

Background of the invention

Tablet dosage forms are the most widely used dosage forms. From the patients point of view they provide unit dose of the active substance accurately, easy to consume and is convenient in storage and transport. From the manufacturers viewpoint, it is economical to manufacture a tablet than any other dosage form. The tablets are available as various types like mouth dissolving tablets, water soluble tablets, dispersible tablets. effervescent tablets, buccal tablets etc. In short they are versatile and can be designed according to the specific requirement of the patient.

It is imperative that a tablet should provide uniform therapeutic levels of the drug with each dose to the patient for maximum efficacy. The drug should be in solution form in the gastrointestinal fluid for absorption. For most tablets, the first important step towards solution is breaking into smaller particles or granules, a process known as disintegration. Thus, the disintegration time of the tablet may give an indication about the extent of the availability of the drug for absorption into systemic circulation. The disintegration time also serves to minimize the batch to batch variability during the manufacturing process. An ideal tablet should have reproducible disintegration time or ultimately reproducible dissolution time for predictable therapeutic effect of the intended dose.

US Patent No. 6,291,462 discloses solid dosage forms of gatifloxacin with reproducible disintegration time comprising a granular phase and an extragranular phase. The granules contain gatifloxacin, fillers, binders and disintegration aids and the extragranular phase contains at least one disintegration aid and a lubricant. The use of an extragranular disintegration aid has been shown to be critical for the reproducible disintegration time of gatifloxacin tablets.

We have now discovered that tablets of gatifloxacin with reproducible disintegration time or dissolution rate can be prepared without using any extragranular disintegration aid.

Summary of the invention

In one general aspect, it relates to a solid oral dosage form of gatifloxacin having an intragranular phase and an extragranular phase wherein the extragranular phase is without any disintegration aid.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising intragranular phase and extragranular phase wherein the intragranular phase comprises gatifloxacin and a wicking agent.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin having an intragranular phase and an extragranular phase wherein the intragranular phase comprises gatifloxacin, wicking agent and one or more auxiliary substance selected from fillers, binders, wicking agent and disintegration aids.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the extragranular phase comprises a water-soluble lubricant.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the extragranular phase comprises a water-soluble filler.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the extragranular phase comprises a water-soluble filler and is without any disintegration aid.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and extragranular phase wherein the intragranular phase comprises gatifloxacin and an ion exchange resin.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the intragranular phase comprises gatifloxacin, ion exchange resin as disintegrant and one or more auxiliary substance selected from the group consisting of fillers, binders, wicking agent and disintegration aid.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the intragranular phase comprises gatifloxacin, polacrillin potassium as a disintegrant and one or more auxiliary substance selected from fillers, binders, wicking agent and disintegration aid.

In another general aspect, it relates to a solid oral dosage form of gatifloxacin comprising an intragranular phase and extragranular phase wherein the intragranular phase comprises gatifloxacin, silicon dioxide as wicking agent and one or more auxiliary substance selected from fillers, binders, wicking agent and disintegration aid.

In yet another general aspect, it relates to a process for the preparation of a solid oral dosage form of gatifloxacin comprising an intragranular phase and extragranular phase wherein the extragranular phase is without any disintegration aid.

In another general aspect, it relates to a process for the preparation of a solid oral dosage form of gatifloxacin wherein the process comprises granulating a blend of gatifloxacin and at least one auxiliary substance selected from fillers, binders, wicking agent and disintegration aid with a granulating liquid, drying and sizing the granules, lubricating and compressing the blend into a tablet.

In another general aspect, it relates to a process for the preparation of solid oral dosage form of gatifloxacin wherein the process comprises blending gatifloxacin and at least one auxiliary substance selected from fillers, binders, wicking agent and disintegration aid, compacting and slugging the above blend, sizing the compacts or slugs to get granules, lubricating and compressing the blend into a tablet.

Detailed Description of the Preferred Embodiments

The term "solid dosage form" as used herein includes tablets or coated tablets, pellets and capsules filled with tablets or pellets prepared as per the embodiments described herein. Particularly suitable solid dosage forms are tablets.

The term "gatifloxacin" as used herein includes gatifloxacin or a pharmaceutically acceptable salt of hydrates there of such as but not limiting to gatifloxacin anhydrous, gatifloxacin hydrochloride, gatifloxacin hemihydrate or sesquihydrate and any other pharmaceutically acceptable form known to the skilled in the art. Generally the amount of gatifloxacin can be from about 20%w/w to about 80% w/w, particularly from about 40%w/w to about 80%w/w of the solid dosage from.

The fillers can be any substance which can provide bulk to the tablet and include without limitation, starch, dicalcium phosphate, calcium carbonate, lactose, mannitol dextrose, sorbitol, sucrose, sodium chloride and combinations thereof. The filler may comprise upto about 40% by weight of the solid dosage form.

The binders can be selected from polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums. The binder may comprise from about 0.1% to about 10% by weight of the solid dosage form.

Wicking agents are the substances which are capable of drawing water into the dosage form and assist in the breaking of the tablets into granules. Any excipient which can serve to transport moisture as discussed above can be considered to be a wicking agent. These agents help in maintaining reproducible disintegration time or drug release rate of the tablets even on ageing. The wicking agent is present in the intragranular phase and include, for example, water soluble excipients like sodium chloride and sugars or sugar alcohols such as dextrose, mannitol, sorbitol, lactose and sucrose; hydrophilic polymers like croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol; silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose. Particularly suitable are silicon dioxide, colloidal silicon dioxide, microcrystalline cellulose and sugars or sugar alcohols. The wicking agent may

comprise from about 1%w/w to about 50%w/w, particularly from about 1%w/w to about 40% w/w of the solid dosage form.

The disintegration aid is present intragranularly and can be selected from the group consisting of ion exchange resins like polacrillin potassium (Amberlite® IRP88) hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and like. Particularly suitable are croscarmellose sodium, sodium starch glycolate and polacrillin potassium. The disintegration aid can be in a concentration of upto about 30%w/w of the solid dosage form.

Lubricants can be talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate and sodium stearyl fumarate. Use of water-soluble lubricant is particularly advantageous. The lubricant may be present in a concentration of about 0.1%w/w to about 5%w/w of the solid dosage form.

The granulating liquid can be, but not limited to, water, ethanol, isopropyl alcohol. acetone, dichloromethane and the like. Alternatively, the binder can be dissolved in the granulating liquid and used as a solution/dispersion.

In one embodiment gatifloxacin tablet may be prepared by

- Blending gatifloxacin and intragranular excipients like filler, binder. wicking agent and disintegrant;
- Granulating the above blend with a granulating liquid;
- Drying and sizing the granules;
- blending the granules with a lubricant and optionally other excipients like fillers and compressing to form a tablet.

In another embodiment gatifloxacin tablets may be prepared by

- Blending gatifloxacin and intragranular excipients like filler, binder, wicking agent and disintegrant;
- compacting or slugging the above blend;
- sizing the compacts or slugs to get granules;
- blending the granules with a lubricant and optionally other excipients like fillers and compressing to form a tablet.

In yet another embodiment gatifloxacin tablet may be prepared by blending gatifloxacin and wicking agent like silicon dioxide, colloidal silicon dioxide and sodium chloride along with binders, fillers and disintegration aid, granulating the blend with a granulating liquid, drying and mixing the granules with lubricant and optionally filler(s) followed by compression to form a tablet.

In still another embodiment gatifloxacin tablet may be prepared by blending gatifloxacin, filler, binder, wicking agent and disintegrant, granulating the blend with a granulating liquid, drying and mixing the granules with sodium stearyl fumarate followed by compression to form a tablet.

In another embodiment gatifloxacin tablet may be prepared by blending gatifloxacin, fillers, binders, wicking agent and disintegration aid, granulating the blend with a granulating liquid, drying and mixing the granules with an extragranular water-soluble filler like lactose, mannitol, dextrose, sorbitol and sucrose and a lubricant followed by compression to form a tablet.

In another embodiment the solid oral dosage form may be prepared by blending gatifloxacin and ion exchange resin, binder, filler and wicking agent; granulating the blend with a granulating liquid, drying and mixing the granules with a lubricant followed by compression to form a tablet.

Tablets can additionally be coated with coating compositions like Opadry® or Lustreclear® sold by Colorcon to impart aesthetic appeal. Such a coating may comprise about 3%w/w by weight of the tablet.

The invention described herein is further illustrated by the following examples but these should not be construed as limiting the scope of the invention.

EXAMPLE 1

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	135
Croscarmellose sodium	70
Povidone	14
Colloidal silicon dioxide	20
Mannitol	47
Purified Water	Q.S.
Extragranular	
Sodium Stearyl Fumarate	14
Total	**700**

Procedure: Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide and mannitol. The above blend was granulated with purified water. The granules were dried, sized and mixed with sodium stearyl fumarate and compressed using appropriate tooling.

EXAMPLE 2

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	98
Croscarmellose sodium	70
Povidone	14
Colloidal silicon dioxide	40
Mannitol	40
Polacrillin potassium	14
Purified Water	Q.S.
Extragranular	
Sodium Stearyl Fumarate	24
Total	**700**

Procedure: Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide, mannitol and polacrillin potassium. The above blend was granulated with purified water. The granules were dried, sized and mixed with sodium stearyl fumarate and compressed using appropriate tooling.

EXAMPLE 3

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	105
Croscarmellose sodium	70
Povidone	7
Colloidal silicon dioxide	40
Mannitol	40
Polacrillin potassium	14
Purified Water	Q.S.
Extragranular	
Lactose	20
Sodium Stearyl Fumarate	24
Total	**720**

Procedure: Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide, mannitol and polacrillin potassium. The above blend was granulated with purified water. The granules were dried, sized and mixed with lactose and sodium stearyl fumarate, compressed using appropriate tooling.

EXAMPLE 4

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	98
Croscarmellose sodium	70
Povidone	7
Colloidal silicon dioxide	40
Mannitol	33
Polacrillin potassium	28
Purified Water	Q.S.
Extragranular	
Mannitol	20
Sodium Stearyl Fumarate	24
Total	**720**

Procedure: Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide, mannitol and polacrillin potassium. The above blend was granulated with purified water. The granules were dried, sized and mixed with mannitol and sodium stearyl fumarate and compressed using appropriate tooling.

The tablets of examples 1 – 4 were subjected to dissolution in a USP type II dissolution apparatus, at 50 rpm in 1000 mL of 0.1 N hydrochloric acid. The dissolution profiles are given in Table 1.

Table 1 Dissolution profiles of tablets of examples 1- 4 measured in a USP type II dissolution apparatus, at 50 rpm in 1000ml of 0.1N hydrochloric acid

Time (min)	% Drug Release			
	Example 1	Example 2	Example 3	Example 4
10	93	98	98	101
20	94	100	99	100
30	94	101	100	100
45	93	101	99	102
60	93	100	102	101

WE CLAIM:

1. A solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the extragranular phase is without any disintegration aid.
2. The oral dosage form according to claim 1 wherein the intragranular phase comprises gatifloxacin and one or more auxiliary substance selected from fillers, binders, wicking agent and disintegration aid and the extragranular phase comprises at least one lubricant.
3. The oral dosage form according to claim 2 wherein the filler is selected from the group consisting of starch, dicalcium phosphate, calcium carbonate. lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.
4. The oral dosage form according to claim 2 wherein the binder is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums.
5. The oral dosage form according to claim 2 wherein the wicking agent is selected from the group consisting of water soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose.
6. The oral dosage form according to claim 5 wherein the wicking agent is a water-soluble excipient.
7. The oral dosage form according to claim 6 wherein the water-soluble excipient is selected from sodium chloride, sugar or sugar alcohols.
8. The oral dosage form according to claim 7 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose and sucrose.
9. The oral dosage form according to claim 5 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol.
10. The oral dosage form according to claim 5 wherein the wicking agent is selected from silicon dioxide and colloidal silicon dioxide.
11. The oral dosage form according to claim 2 wherein the disintegration aid is selected from the group consisting of ion exchange resins,

hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and like.

12. The oral dosage form according to claim 11 wherein the disintegration aid is croscarmellose sodium.

13. The oral dosage form according to claim 11 wherein the disintegration aid is an ion exchange resin.

14. The oral dosage form according to claim 13 wherein the ion exchange resin is polacrillin potassium.

15. The oral dosage form according to claim 2 wherein the lubricant is selected from the group consisting of talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate and sodium stearyl fumarate.

16. The oral dosage from according to claim 15 wherein the lubricant is sodium stearyl fumarate.

17. The oral dosage form according to claim 2 wherein the extragranular phase further comprises a water soluble filler.

18. The oral dosage form according to claim 17 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.

19. A solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the intragranular phase comprises gatifloxacin and a wicking agent.

20. The oral solid dosage form according to claim 19 wherein the extragranular phase is without disintegration aid.

21. The oral dosage form according to claim 19 or 20 wherein the wicking agent is selected from the group consisting of water-soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose.

22. The oral dosage form according to claim 21 wherein the water-soluble excipient is selected from sodium chloride, sugar or sugar alcohols.

23. The oral dosage form according to claim 22 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose and sucrose.

24. The oral dosage form according to claim 21 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone,

starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol.

25. The oral dosage form according to claim 21 wherein the wicking agent is selected from silicon dioxide and colloidal silicon dioxide.

26. The solid oral dosage according to claim 19 or 20 wherein the intragranular phase further comprises one or more auxiliary substance selected from fillers, binders and disintegration aid and the extragranular phase comprises at least one lubricant.

27. The oral dosage form according to claim 26 wherein the filler is selected from the group consisting of starch, dicalcium phosphate, calcium carbonate. lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.

28. The oral dosage form according to claim 26 wherein the binder is selected from the group consisting of polyvinylpyrrolidone. hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage. carbopols and gums.

29. The oral dosage form according to claim 26 wherein the disintegration aid is selected from the group consisting of ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium. starches. pectins, alginates, surfactants, microcrystalline cellulose. sodium starch glycolate and like.

30. The oral dosage form according to claim 29 wherein the disintegration aid is croscarmellose sodium.

31. The oral dosage form according to claim 29 wherein the disintegration aid is an ion exchange resin.

32. The oral dosage form according to claim 29 wherein the ion exchange resin is polacrillin potassium.

33. The oral dosage form according to claim 26 wherein the lubricant is selected from the group consisting of talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate and sodium stearyl fumarate.

34. The oral dosage form according to claim 30 wherein the lubricant is sodium stearyl fumarate.

35. The oral dosage form according to claim 26 wherein the extragranular phase further comprises a water soluble filler.

36. The oral dosage form according to claim 35 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.

37. A solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the extragranular phase comprises a water-soluble lubricant.

38. The oral dosage form according to claim 37 wherein the extragranular phase is without any disintegration aid.

39. The solid dosage form according to 37 or 38 wherein the water soluble lubricant is selected from sodium stearyl fumarate, polyethylene glycol and sodium chloride.

40. The solid dosage form according to claim 39 wherein the lubricant is sodium stearyl fumarate.

41. The oral dosage form according to claim 37 or 38 wherein the extragranular phase further comprises a water soluble filler.

42. The oral dosage form according to claim 41 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.

43. The oral dosage form according to claim 37 or 38 wherein the intragranular phase comprises gatifloxacin and one or more auxiliary substance selected from fillers, binders, wicking agent and disintegration aid.

44. The oral dosage form according to claim 43 wherein the filler is selected from the group consisting of starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.

45. The oral dosage form according to claim 43 wherein the binder is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums.

46. The oral dosage form according to claim 43 wherein the wicking agent is selected from the group consisting of water soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose.

47. The oral dosage form according to claim 46 wherein the water-soluble excipient is selected from sodium chloride, sugar or sugar alcohols.

48. The oral dosage form according to claim 47 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose and sucrose.

49. The oral dosage form according to claim 46 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol.

50. The oral dosage form according to claim 46 wherein the wicking agent is selected from silicon dioxide and colloidal silicon dioxide.

51. The oral dosage form according to claim 43 wherein the disintegration aid is selected from the group consisting of ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and like.

52. The oral dosage form according to claim 51 wherein the disintegration aid is croscarmellose sodium.

53. The oral dosage form according to claim 51 wherein the disintegration aid is an ion exchange resin.

54. The oral dosage form according to claim 53 wherein the ion exchange resin is polacrillin potassium.

55. A solid oral dosage form of gatifloxacin comprising an intragranular phase and extragranular phase wherein the extragranular phase comprises a water soluble filler.

56. The oral dosage form according to claim 55 wherein the extragranular phase is without any disintegration aid.

57. The oral dosage form according to claim 55 or 56 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.

58. The solid dosage form according to claim 57 wherein the water soluble filler is lactose.

59. The oral dosage form according to claim 57 wherein the water soluble filler is mannitol.

60. The solid dosage form according to claim 55 or 56 wherein the extragranular phase further comprises a lubricant.

61. The oral dosage form according to claim 60 wherein the lubricant is selected from the group consisting of talc, polyethylene glycol, sodium chloride, stearic

acid, calcium stearate, zinc stearate, magnesium stearate and sodium stearyl fumarate.

62. The oral dosage form according to claim 61 wherein the lubricant is sodium stearyl fumarate.

63. The oral dosage form according to claim 55 or 56 wherein the intragranular phase comprises gatifloxacin and one or more auxiliary substance selected from fillers, binders, wicking agent and disintegration aid.

64. The oral dosage form according to claim 63 wherein the filler is selected from the group consisting of starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.

65. The oral dosage form according to claim 63 wherein the binder is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums.

66. The oral dosage form according to claim 63 wherein the wicking agent is selected from the group consisting of water soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose.

67. The oral dosage form according to claim 66 wherein the water-soluble excipient is selected from sodium chloride, sugar or sugar alcohols.

68. The oral dosage form according to claim 67 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose and sucrose.

69. The oral dosage form according to claim 66 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol.

70. The oral dosage form according to claim 66 wherein the wicking agent is selected from silicon dioxide and colloidal silicon dioxide.

71. The oral dosage form according to claim 63 wherein the disintegration aid is selected from the group consisting of ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and like.

72. The oral dosage form according to claim 71 wherein the disintegration aid is croscarmellose sodium.

73. The oral dosage form according to claim 71 wherein the disintegration aid is an ion exchange resin.

74. The oral dosage form according to claim 73 wherein the ion exchange resin is polacrillin potassium.

75. A solid oral dosage form of gatifloxacin comprising intragranular phase and extragranular phase wherein the intragranular phase comprises ion exchange resin as disintegration aid.

76. The oral dosage form according to claim 75 wherein the extragranular phase is without disintegration aid.

77. The oral dosage form according to claim 75 or 76 wherein the ion exchange resin is polacrillin potassium.

78. The oral dosage form according to claim 75 or 76 wherein the intragranular phase further comprises gatifloxacin and one or more of auxiliary substances selected from fillers, binders, wicking agent and optionally other disintegration aid.

79. The oral dosage form according to claim 78 wherein the filler is selected from the group consisting of starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.

80. The oral dosage form according to claim 78 wherein the binder is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums.

81. The oral dosage form according to claim 78 wherein the wicking agent is selected from the group consisting of water soluble excipient, hydrophilic polymers, silicon dioxide and microcrystalline cellulose.

82. The oral dosage form according to claim 81 wherein the wicking agent is a water-soluble excipient.

83. The oral dosage form according to claim 82 wherein the water-soluble excipient is selected from sodium chloride, sugar or sugar alcohols.

84. The oral dosage form according to claim 83 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose and sucrose.

85. The oral dosage form according to claim 81 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol.

86. The oral dosage form according to claim 81 wherein the wicking agent is selected from silicon dioxide and colloidal silicon dioxide.

87. The oral dosage form according to claim 78 wherein the other disintegration aid is selected from the group consisting of hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and like.

88. The oral dosage form according to claim 87 wherein the disintegration aid is croscarmellose sodium.

89. The oral dosage form according to claim 75 or 76 wherein the extragranular phase comprises at least one lubricant.

90. The oral dosage form according to claim 89 wherein the lubricant is selected from the group consisting of talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate, and sodium stearyl fumarate.

91. The oral dosage form according to claim 90 wherein the lubricant is sodium stearyl fumarate.

92. The oral dosage form according to claim 89 wherein the extragranular phase further comprises a water soluble filler.

93. The oral dosage form according to claim 92 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.

94. A process for the preparation of a solid oral dosage form of gatifloxacin comprising an intragranular phase and an extragranular phase wherein the extragranular phase is without any disintegration aid.

95. The process according to claim 94 wherein the process comprises granulating a blend of gatifloxacin and one or more of auxiliary substance selected from fillers, binders, wicking agent and disintegration aid, lubricating the granules with a lubricant and compressing into a solid dosage form.

96. The process according to claim 95 wherein the granulation is done by wet granulation method.

97. The process according to claim 96 wherein the granulation is carried out by granulating liquid selected from the group consisting of water, ethanol, isopropyl alcohol, acetone, dichloromethane and the like or a binder solution.

98. The process according to claim 95 wherein the granulation is done by dry granulation method.

99. The process according to claim 98 wherein the dry granulation is carried out by compaction or slugging.

100. The process according to claim 99 wherein the granulation is carried out by compaction.

101. The process according to claim 95 wherein the filler is selected from the group consisting of starch, dicalcium phosphate, calcium carbonate. lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.

102. The process according to claim 95 wherein the binder is selected from the group consisting of polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums.

103. The process according to claim 95 wherein the wicking agent is selected from the group consisting of water soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose.

104. The process according to claim 103 wherein the wicking agent is a water-soluble excipient.

105. The process according to claim 104 wherein the water-soluble excipient is selected from sodium chloride, sugar or sugar alcohols.

106. The process according to claim 105 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose and sucrose.

107. The process according to claim 103 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol.

108. The oral dosage form according to claim 103 wherein the wicking agent is selected from silicon dioxide and colloidal silicon dioxide.

109. The process according to claim 95 wherein the disintegration aid is selected from the group consisting of ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and like.

110. The process according to claim 109 wherein the disintegration aid is croscarmellose sodium.

111. The process according to claim 109 wherein the disintegration aid is an ion exchange resin.

112. The process according to claim 111 wherein the ion exchange resin is polacrillin potassium.

113. The process according to claim 95 wherein the lubricant is selected from the group consisting of talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate and sodium stearyl fumarate.

114. The process according to claim 113 wherein the lubricant is sodium stearyl fumarate.

115. The process according to claim 95 wherein the process further comprises adding an extragranular water soluble filler.

116. The process according to claim 115 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.

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For Ranbaxy Laboratories Limited

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ABSTRACT

The present invention relates to solid oral dosage forms of gatifloxacin having reproducible release characteristics and processes for the preparation thereof.